CLAIMS

1. A compound of the formula (I):

$$R^1—NH—X—Y—Z \quad (I)$$

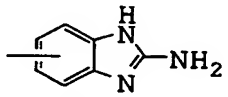
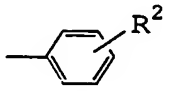
wherein

R^1 is acyl;

X is a bivalent residue derived from optionally substituted thiazole;

Y is a bond, lower alkylene, lower alkenylene or -CONH-; and

Z is a group of the formula:

 or 

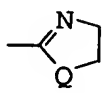
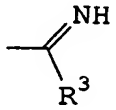
wherein R^2 is a group of the formula: -A-B-D-E

wherein A is a bond, lower alkylene, -NH- or $-SO_2-$;

B is a bond, lower alkylene, -CO- or -O-;

D is a bond, lower alkylene, -NH- or $-CH_2NH-$; and

E is optionally protected amino, $-N=CH_2$,

 or 

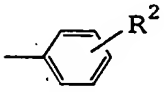
wherein

Q is -S- or -NH-; and

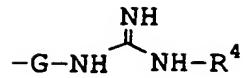
R^3 is hydrogen, lower alkyl, lower alkylthio or $-NH-R^4$ wherein R^4 is hydrogen, $-NH_2$ or lower alkyl;

or a pharmaceutically acceptable salt thereof.

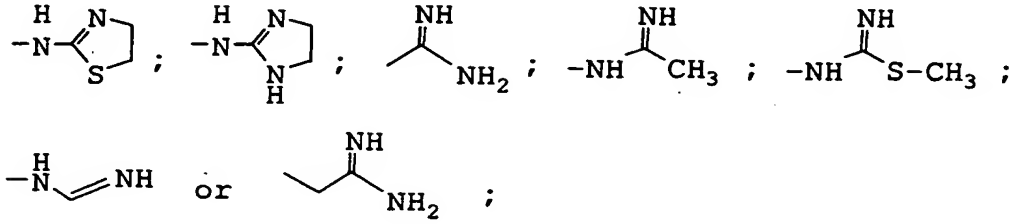
2. The compound of claim 1, wherein Z is a group of the formula:



wherein R^2 is a group of the formula:

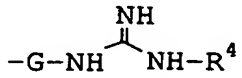


(wherein G is a bond, $-NHCOCH_2-$ or lower alkylene and R^4 is hydrogen, $-NH_2$ or lower alkyl); $-NH_2$; $-CH_2NH_2$; $-CH_2ONH_2$; $-CH_2ON=CH_2$;

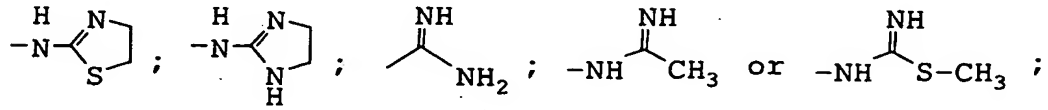


or a pharmaceutically acceptable salt thereof.

3. The compound of claim 2, wherein R^2 is a group of the formula:



(wherein G is a bond, $-NHCOCH_2-$ or lower alkylene and R^4 is hydrogen or lower alkyl); $-CH_2NH_2$; $-CH_2ONH_2$; $-CH_2ON=CH_2$;



or a pharmaceutically acceptable salt thereof.

4. The compound of any of claims 1 to 3, wherein R^1 is alkylcarbonyl and X is a bivalent residue derived from thiazole optionally substituted by methylsulfonylbenzyl, or a pharmaceutically acceptable salt thereof.

5. The compound of claim 1, wherein the compound is
N-{4-[2-(4-{[amino(imino)methyl]amino}phenyl)ethyl]-1,3-thiazol-2-yl}acetamide,
N-{4-[2-(4-{[amino(imino)methyl]amino}phenyl)ethyl]-5-[4-(methylsulfonyl)benzyl]-1,3-thiazol-2-yl}acetamide,

N-{4-[2-(4-{[hydrazino(imino)methyl]amino}phenyl)ethyl]-5-[4-(methylsulfonyl)benzyl]-1,3-thiazol-2-yl}acetamide,
N-{4-[2-(4-{[hydrazino(imino)methyl]amino}phenyl)ethyl]-1,3-thiazol-2-yl}acetamide, or
N-(4-{2-[4-(2-{[amino(imino)methyl]amino}ethyl)phenyl]ethyl}-1,3-thiazol-2-yl)acetamide,
or a pharmaceutically acceptable salt thereof.

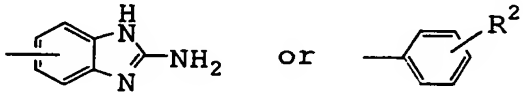
6. The compound of claim 1 or a pharmaceutically acceptable salt thereof for use as a medicament.

7. A pharmaceutical composition, which comprises, as an active ingredient, the compound of claim 1 or a pharmaceutically acceptable salt thereof.

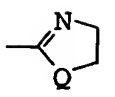
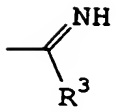
8. A method for producing a compound of the formula (I):

$$R^1—NH—X—Y—Z \quad (I)$$

wherein
R^1 is acyl;
X is a bivalent residue derived from optionally substituted thiazole;
Y is a bond, lower alkylene, lower alkenylene or -CONH-; and
Z is a group of the formula:

 or

wherein R^2 is a group of the formula: -A-B-D-E
wherein A is a bond, lower alkylene, -NH- or $-SO_2-$;
B is a bond, lower alkylene, -CO- or -O-;
D is a bond, lower alkylene, -NH- or $-CH_2NH-$; and
E is optionally protected amino, $-N=CH_2$,

 or 

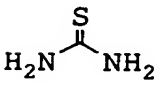
wherein

Q is -S- or -NH-; and

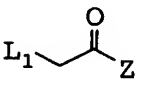
R^3 is hydrogen, lower alkyl, lower alkylthio or $-NH-R^4$ wherein R^4 is hydrogen, $-NH_2$ or lower alkyl;

or a pharmaceutically acceptable salt thereof, which method comprises at least one step selected from the group consisting of (i) to (v):

(i) reacting Compound (1):



with Compound (2):



wherein L_1 is a leaving group and Z is as defined above, or a salt thereof;

(ii) reacting Compound (3): H_2N-X-Z

wherein X and Z are as defined above, or a salt thereof with Compound (4): R^1-L_2

wherein R^1 is as defined above and L_2 is a leaving group;

(iii) reacting Compound (6): $R^1-NH-X-CHO$

wherein R^1 and X are as defined above, or a salt thereof with Compound (7): L_3-CH_2-Z

wherein L_3 is a leaving group and Z is as defined above, or a salt thereof;

(iv) reduction of Compound (10): $R^1-NH-X-$(lower alkenylene)$-Z$

wherein R^1, X and Z are as defined above, or a salt thereof to Compound (11): $R^1-NH-X-$(lower alkylene)$-Z$

wherein R^1, X and Z are as defined above, or a salt thereof; and

(v) reacting Compound (12): R^1-NH-X-COOH or a reactive derivative thereof, wherein R^1 and X are as defined above, or a salt thereof with Compound (13): L_4-NH-Z wherein L^4 is a hydrogen atom or a protecting group and Z is as defined above, or a salt thereof.

9. A use of the compound of claim 1 or a pharmaceutically acceptable salt thereof for preparing a medicament as a VAP-1 inhibitor.

10. The use of claim 9, wherein the compound is
N-{4-[2-(4-{[amino(imino)methyl]amino}phenyl)ethyl]-1,3-thiazol-2-yl}acetamide,
N-{4-[2-(4-{[amino(imino)methyl]amino}phenyl)ethyl]-5-[4-(methylsulfonyl)benzyl]-1,3-thiazol-2-yl}acetamide,
N-{4-[2-(4-{[hydrazino(imino)methyl]amino}phenyl)ethyl]-5-[4-(methylsulfonyl)benzyl]-1,3-thiazol-2-yl}acetamide,
N-{4-[2-(4-{[hydrazino(imino)methyl]amino}phenyl)ethyl]-1,3-thiazol-2-yl}acetamide, or
N-(4-{2-[4-(2-{[amino(imino)methyl]amino}ethyl)phenyl]ethyl}-1,3-thiazol-2-yl)acetamide.

11. A use of the compound of claim 1 or a pharmaceutically acceptable salt thereof for preparing a medicament for the prophylaxis or treatment of a VAP-1 associated disease.

12. The use of claim 11, wherein said VAP-1 associated disease is selected from the group consisting of cirrhosis, essential stabilized hypertension, diabetes, arthrosis, endothelium damage (in diabetes, atherosclerosis and hypertension), a cardiovascular disorder associated with diabetes and uraemia, pain associated with gout and arthritis, retinopathy (in diabetes patients), an (connective tissue) inflammatory

disease or condition (rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis and osteoarthritis or degenerative joint disease, Reiter's syndrome, Sjögren's syndrome, Behçet's syndrome, relapsing polychondritis, systemic lupus erythematosus, discoid lupus erythematosus, systemic sclerosis, eosinophilic fasciitis, polymyositis, dermatomyositis, polymyalgia rheumatica, vasculitis, temporal arteritis, polyarteritis nodosa, Wegener's granulomatosis, mixed connective tissue disease, and juvenile rheumatoid arthritis), a gastrointestinal inflammatory disease or condition [Crohn's disease, ulcerative colitis, irritable bowel syndrome (spastic colon), fibrotic conditions of the liver, inflammation of the oral mucosa (stomatitis), and recurrent aphtous stomatitis], a central nervous system inflammatory disease or condition (multiple sclerosis, Alzheimer's disease, and ischaemia-reperfusion injury associated with ischemic stroke), a pulmonary inflammatory disease or condition (asthma, adult respiratory distress syndrome, chronic obstructive pulmonary disease), a (chronic) skin inflammatory disease or condition (psoriasis, allegic lesions, lichen planus, pityriasis rosea, contact dermatitis, atopic dermatitis, pityriasis rubra pilaris), a disease related to carbohydrate metabolism (diabetes and complications from diabetes) including microvascular and macrovascular disease (atherosclerosis, vascular retinopathies, retinopathy, nephropathy, nephrotic syndrome and neuropathy (polyneuropathy, mononeuropathies and autonomic neuropathy), foot ulcers, joint problems, and increased risk of infection), a disease related to aberrations in adipocyte differentiation or function or smooth muscle cell function (atherosclerosis and obesity), a vascular disease [atheromatous ateriosclerosis, nonatheromatous ateriosclerosis, ischemic heart disease including myocardial infarction and peripheral arterial

occlusion, Raynaud's disease and phenomenon, thromboangiitis obliterans (Buerger's disease)], chronic arthritis, inflammatory bowel diseases, skin dermatoses, diabetes mellitus, SSAO-mediated complication [diabetes (insulin dependent diabetes mellitus (IDDM) and non-insulin dependent diabetes mellitus (NIDDM)) and vascular complication (heart attack, angina, strokes, amputations, blindness and renal failure)] and macular edema (diabetic and non-diabetic macular edema).

13. The use of claim 12, wherein said VAP-1 associated disease is macular edema.

14. The use of claim 13, wherein said macular edema is diabetic macular edema.

15. The use of claim 13, wherein said macular edema is non-diabetic macular edema.

16. A VAP-1 inhibitor, which comprises the compound of claim 1 or a pharmaceutically acceptable salt thereof.

17. A method for preventing or treating macular edema, which method comprises administering to a subject in need thereof a VAP-1 inhibitor in an amount sufficient to treat said subject for macular edema.

18. The method of claim 17, wherein the VAP-1 inhibitor is
N-{4-[2-(4-{[amino(imino)methyl]amino}phenyl)ethyl]-1,3-thiazol-2-yl}acetamide,
N-{4-[2-(4-{[amino(imino)methyl]amino}phenyl)ethyl]-5-[4-(methylsulfonyl)benzyl]-1,3-thiazol-2-yl}acetamide,
N-{4-[2-(4-{[hydrazino(imino)methyl]amino}phenyl)ethyl]-5-[4-

(methylsulfonyl)benzyl]-1,3-thiazol-2-yl}acetamide,
N-{4-[2-(4-{[hydrazino(imino)methyl]amino}phenyl)ethyl]-1,3-thiazol-2-yl}acetamide, or
N-(4-{2-[4-(2-{[amino(imino)methyl]amino}ethyl)phenyl]ethyl}-1,3-thiazol-2-yl)acetamide,
or a pharmaceutically acceptable salt thereof.

19. A method for preventing or treating a VAP-1 associated disease, which method comprises administering an effective amount of the compound of claim 1 or a pharmaceutically acceptable salt thereof to a mammal.

20. The method of claim 19, wherein said VAP-1 associated disease is selected from the group consisting of cirrhosis, essential stabilized hypertension, diabetes, arthrosis, endothelium damage (in diabetes, atherosclerosis and hypertension), a cardiovascular disorder associated with diabetes and uraemia, pain associated with gout and arthritis, retinopathy (in diabetes patients), an (connective tissue) inflammatory disease or condition (rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis and osteoarthritis or degenerative joint disease, Reiter's syndrome, Sjögren's syndrome, Behçet's syndrome, relapsing polychondritis, systemic lupus erythematosus, discoid lupus erythematosus, systemic sclerosis, eosinophilic fasciitis, polymyositis, dermatomyositis, polymyalgia rheumatica, vasculitis, temporal arteritis, polyarteritis nodosa, Wegener's granulomatosis, mixed connective tissue disease, and juvenile rheumatoid arthritis), a gastrointestinal inflammatory disease or condition [Crohn's disease, ulcerative colitis, irritable bowel syndrome (spastic colon), fibrotic conditions of the liver, inflammation of the oral mucosa (stomatitis), and

recurrent aphtous stomatitis], a central nervous system inflammatory disease or condition (multiple sclerosis, Alzheimer's disease, and ischaemia-reperfusion injury associated with ischemic stroke), a pulmonary inflammatory disease or condition (asthma, adult respiratory distress syndrome, chronic obstructive pulmonary disease), a (chronic) skin inflammatory disease or condition (psoriasis, allegic lesions, lichen planus, pityriasis rosea, contact dermatitis, atopic dermatitis, pityriasis rubra pilaris), a disease related to carbohydrate metabolism (diabetes and complications from diabetes) including microvascular and macrovascular disease (atherosclerosis, vascular retinopathies, retinopathy, nephropathy, nephrotic syndrome and neuropathy (polyneuropathy, mononeuropathies and autonomic neuropathy), foot ulcers, joint problems, and increased risk of infection), a disease related to aberrations in adipocyte differentiation or function or smooth muscle cell function (atherosclerosis and obesity), a vascular disease [atheromatous ateriosclerosis, nonatheromatous ateriosclerosis, ischemic heart disease including myocardial infarction and peripheral arterial occlusion, Raynaud's disease and phenomenon, thromboangiitis obliterans (Buerger's disease)], chronic arthritis, inflammatory bowel diseases, skin dermatoses, diabetes mellitus, SSAO-mediated complication [diabetes (insulin dependent diabetes mellitus (IDDM) and non-insulin dependent diabetes mellitus (NIDDM)) and vascular complication (heart attack, angina, strokes, amputations, blindness and renal failure)] and macular edema (diabetic and non-diabetic macular edema).

21. The method of claim 20, wherein said VAP-1 associated disease is macular edema.

22. The method of claim 21, wherein said macular edema is diabetic macular edema.

23. The method of claim 21, wherein said macular edema is non-diabetic macular edema.